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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,729	11/13/2001	Moses Rodriguez	1199-1-005CIP2	4304

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KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 12/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,729	RODRIGUEZ ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-90* is/are pending in the application.

4a) Of the above claim(s) *1-41,44-61,64,66-72 and 74-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,43,62,63,65 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-90* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks and election filed 28 March 2005 and substitute sequence listing filed 21 September 2005 have been entered. Claims 1 – 90 are pending.

2. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Election/Restrictions

3. Applicant's election with traverse of Group IV, and LYM22 as the specific antibody in the reply filed on 28 March is acknowledged. The traversal is on the ground(s) that the antibodies and the nucleic acids that encode them are not patentably distinct, that search of DNAs and antibodies together is not burdensome, and that search for all antibodies together is not burdensome. This is not found persuasive for the following reasons.

1) DNA and antibodies are patentably distinct products. Antibodies are polypeptides, comprised of amino acids whereas DNA is a nucleic acid. Consideration of DNA inventions requires search of nucleic acid databases, which is not informative as to the novelty of an antibody. Consideration of antibodies requires search of the patent and non-patent literature for disclosure of the antibodies. Thus consideration of these two patentably distinct inventions would require two separate searches and would be burdensome for the examiner. Applicant argues that search of the classes containing antibodies would overlap with the classes containing DNAs, but this is not true. Antibodies are classified in 530/388.1, whereas DNAs are classified in 536, 23.1.

2) Each antibody is a patentably distinct molecule because it binds to a different antigen. Antibodies which bind to different antigens cannot be substituted one for the other and thus are patentably distinct. Furthermore search for any one antibody, either by name or by sequence to which it binds, would not be informative as to the patentability of any other antibody. So consideration of more than one antibody would require a separate search and would be burdensome to the examiner.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 1 – 41, 44 – 61, 64, 66 – 72, and 74 – 90 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 28 March 2005.

5. Claims 42 – 43, 62 – 63, 65, and 73 are under examination.

Priority Determination

6. 35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

7. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. The instant application is a continuation-in-part of 09/730473, which is a continuation-in-part of 09/580787, which is a continuation-in-part of 09/322862, which is a continuation-in-part of 08779784, which is a continuation of 08/692,084, which is a continuation-in-part of 08/236520, now U.S. Patent 5,591,629. The examiner is able to find disclosure of the sHIgM22 antibody in 09/322,862, for example at page 3 of the specification. However the examiner is not able to find support for this product in any of the earlier-filed applications. Therefore the effective filing date of all claims under examination is 28 May 1999, the date that 09/322862 was filed.

Should applicant disagree with the factual determination above, applicant should indicate why an earlier-filed application does in fact constitute an enabling disclosure. This could be accomplished, for example, by pointing out the specific page and line numbers in the earlier-filed applications where support can be found for the instantly-claimed invention.

Claim Objections

8. Claims 42, 62 – 63, 65, and 73 are objected to because of the following informalities: they recite non-elected subject manner. Specifically, claim 42 recites sHIgM46 (LYM46), cbvHIgM MS119d10, Cb2BG8, MSI10L10, as well as the antigens to which all antibodies bind. Claim 62 recites Figure 71 (SEQ ID NO:49), Figure 72 (SEQ ID NO:51), which are not related to the instantly-elected invention. Claim 73 is under examination to the extent that it reads on the instantly-elected antibody, regardless of the actual language of the claim. No peptide antigen has been described, and furthermore binding partners are beyond the scope of antibodies, which have been elected by applicant. Furthermore claim 73 depends from multiple non-elected claims which encompass non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Utility is acknowledged because the specification discloses that the sHIgM22 antibody promotes remyelination *in vivo* (pp. 129-130 and 136). The antibody promotes remyelination in mice infected with TMEV; this is an art-accepted model of multiple sclerosis (see Luizzi et al. 1995. Journal of Neuroimmunology 62:91-102, particularly fist page).

11. Claims 42 – 43, 62 – 63. 65, and 73 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims encompass sHIgM22 antibody. This is a product of nature. Ciric et al. (2001.) Blood 97:321-323 teaches isolation of sHIgM 22 from patient plasma; blood and plasma are both pharmaceutically acceptable carriers thus the claims read on the naturally occurring product. Amendment to "isolated" antibodies is recommended.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 42, 62 – 63, 65, and 73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions comprising the

monoclonal antibody SHIgM22, does not reasonably provide enablement for compositions comprising all active fragments, binding partners, and antibodies derived therefrom. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

In the instant case, the nature of the invention, monoclonal antibodies which promote remyelination, is complex. See Alberts et al., 1994. Molecular Biology of the Cell, pp. 1206 – 1216 for a review of the complex nature of antibodies. The claims are broad in that they encompass an essentially unlimited number of fragments, binding partners, and antibodies derived from the parent antibody, without any limit on structure or function. For example claims 42 and 62 encompass all "active fragments" but there is no recitation of what constitutes active, nor is there a definition in the specifcation. Thus the claim reasonably includes all fragments which have any activity, including those that do not bind to the target antigen. Furthermore claim 42 includes all binding partners, which can either be the antigen itself, or a molecule that binds to the Fc portion of the antibody. However the specification fails to disclose the active fragments and binding partners as broadly claimed. The antibody was not made by injecting a known peptide into a host and then isolating the antibodies which bind to said peptide; it was isolated from a human patient (see Ciric et al. 2001. Blood 97:321-323). Even the post-filing publications by Ciric, which includes two of the three inventors of the instant application, fails to identify the binding partner of the antibody. Thus the skilled artisan would have to resort to undue experimentation in order to make and use the binding partners of the antibody.

The specification also fails to disclose any recombinant antibodies derived from sHIgM22. There are no requirements in the claims that any particular structure be present, or any function. Given the lack of guidance, combined with the complex nature of the invention,

and the breadth of the claims, there would be an undue burden on the skilled artisan to make and use the invention as claimed.

14. Claims 42 – 43, 62 – 63, 65, and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The examiner has determined that in order for a skilled artisan to make the claimed antibodies, the artisan must have access to the hybridoma that produces the antibodies. The specification does not provide sufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposit was made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State. Additionally, amendment of the specification to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line is required.

15. Claims 42, 62-63, 65, and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are broad in that they include all possible active fragments, wherein activity is not specified, all binding partners of undisclosed structure or function (claim 42), as well as antibodies which could be obtained through recombinant technology. However what is disclosed, the antibody named sHIgM22 (LYM22) is narrow. The specification fails to disclose the active fragments and binding partners as broadly claimed. The antibody was not made by injecting a known peptide into a host and then isolating the antibodies which bind to said peptide; it was isolated from a human patient (see Ciric et al. 2001. Blood 97:321-323). Even

the post-filing publications by Ciric, which includes two of the three inventors of the instant application, fails to identify the binding partner of the antibody. Thus the specification does not reasonably provide support for binding partners and active fragments as claimed. The specification does not disclose a reasonable number of members of the claimed genera and sub-genera.

The instant disclosure of a single antibody, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606." While the above quotation from *Fiers* is drawn to DNAs, the same logic applies to antibodies.

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 62 - 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 62 is drawn to antibody produced by injecting a peptide comprising SEQ ID NO:9 or 10. The specification indicates that Figures 35 and 36 are the heavy and light chain variable regions, respectively, of sHIgM22 (see pp. 29 – 30). However SEQ ID NO:8 and 10 are not peptide sequences, they are nucleic acid sequences. Thus the skilled artisan could not determine the metes and bounds of the claim, as it is unclear whether the nucleic acid comprising SEQ ID NO:8 or 10 is to be injected, or whether an amino acid encoded by said nucleic acid is to be injected to the substantially immunocompetent host.

Claim 65 recites the terms "chimeric (bi-specific)", implying the two terms are identical and interchangeable. However neither term is explicitly defined in the specification. A bi-specific antibody is defined in Ho et al. (U.S. Patent 5,770,567, issued 23 June 1998) as one that binds to two antigens (see paragraph spanning columns 47 – 48), whereas chimeric antibodies are comprised of antibody fragments from two different species (see Ho, column 45, lines 30 – 39). Clearly the two-terms are not of identical scope, and thus the artisan would not be able to determine the metes and bounds of the claim.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 42, 62 – 63, 65 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by Alberts (et al., 1994. Molecular Biology of the Cell, pp. 187-188, 1206 – 1216.), as evidenced by Queen (U.S. Patent 5,693,762, issued 2 December 1997, earliest effective filing date 28 December 1988). The claims include "active fragments" of antibodies. Alberts teaches Fc fragments (p. 1209) which are active in that they contain the region which binds to C1 complex (see p. 1214). Furthermore Alberts teaches monoclonal antibodies (pp. 187 – 188) and since these are derived from cells which produce antibodies, the teachings on p. 1209 also

apply to monoclonals. Queen teaches that chimeric antibodies are comprised of regions from two different antibodies, which when combined form an intact antibody (see column 3 lines 33 – 43 for example), and thus provides evidence that the active fragments taught by Alberts apply to chimeric antibodies as well. As claim 73 is a product-by-process claim which is sufficiently broad to include Fc fragments (see claim 46 line 3, from which 73 ultimately depends), it stands rejected as well.

Conclusion

20. No claim is allowed.

21. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

1) Ciric et al. (2001), Blood 97:321-323 teaches isolation of sHIgM 22 from patient plasma.

2) Warrington et al. (2000). Proc Natl Acad Sci USA 97:6820-6825 teach isolation of sHIgM22 antibody from human samples.

Both references were published after the effective filing date for this application.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.

SHARON TURNER, PH.D.
PRIMARY EXAMINER
11-28-05